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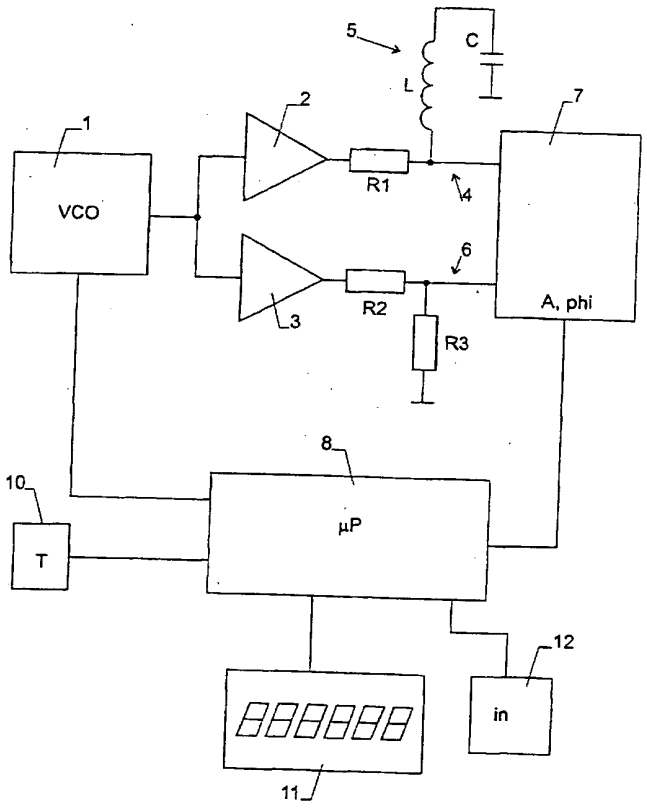
(54) Title: METHOD AND DEVICE FOR DETERMINING THE CONCENTRATION OF A SUBSTANCE IN BODY LIQUID



(57) Abstract: For measuring the concentration of a substance in body fluid, such as the glucose level in blood or tissue, a strip electrode (18) and a ring electrode (19) are arranged at the specimen. The ring electrode (19) is in direct electrical contact with the specimen while the strip electrode (18) is electrically insulated therefrom. The strip electrode (18) is arranged parallel to an arm or a leg for obtaining a large interaction length. The electrodes (18, 19) form a capacitor in a resonant circuit. A modulated voltage in the MHz range close to or at the resonance frequency is applied to the electrodes and the response of the body fluid is measured. This design allows a measurement of high accuracy.

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Method and device for determining the concentration of a substance in body liquid

Technical Field

The invention relates to a method and a device for determining the concentration of a substance in an in-vitro or in-vivo specimen containing body liquid according to the preamble of the independent claims.

Background Art

Radio wave spectroscopy has been known to provide promising potential in the in-vitro and in-vivo determination of the concentration of glucose and other substances in body fluids. In particular, this technology is of substantial interest for the determination of glucose concentration in blood and/or inter- or intracellular liquid. A device for measuring blood level glucose is disclosed in US 5 792 668, where two electrodes are brought into direct contact with the human body and the impedance is measured between them.

Despite its potential, the technology has not yet been used in commercial devices, which is attributed to the limited accuracy of the presently known solutions.

Disclosure of the Invention

Hence, it is the goal of the invention to provide a method and device that allow to increase the reliability of this type of measurement.

This goal is reached by the independent claims.

In a first aspect of the invention, the first electrode is electrically insulated from the specimen.

The method and device of the present invention has been found to be especially suited for measuring the glucose concentration in body fluid.

Brief Description of the Drawings

The invention will be better understood and objects other than those set forth above will become apparent when consideration is given to the following detailed description thereof. Such description makes reference to the annexed drawings, wherein:

Fig. 1 is a block circuit diagram of a preferred device for carrying out the invention,

Fig. 2 is a view onto a possible embodiment of the device,

Fig. 3 is a section along line III-III of Fig. 2,

Fig. 4 is the device of Fig. 3 with a wristband,

Fig. 5 shows the behavior of the relative amplitude A as a function of frequency,

Fig. 6 is a second embodiment of the circuit,

Fig. 7 is an alternative electrode geometry,

Fig. 8 shows measurements at varying glucose concentrations (mmol/liter) in physiologic solution and

Fig. 9 a third embodiment of the circuit.

Modes for Carrying Out the Invention

Fig. 1 shows a block circuit diagram of a preferred device for carrying out the invention. It comprises a voltage controlled oscillator (VCO) 1 as a signal source for generating a sine wave signal. This signal is fed to two amplifiers 2, 3. The output of first amplifier 2 is connected via a resistor R1 to a first signal

on the electrical properties (i.e. the response) of the specimen at the frequency of VCO 1.

To measure the concentration of a substance in the body fluid of the specimen, microprocessor 8 can e.g. initiate a measurement cycle consisting of a frequency sweep of VCO 1. The sweep should start at a frequency fmin below the expected resonance frequency f0 of the resonant circuit 5 and extend to a frequency fmax above resonance frequency f. During this sweep, the electrical properties of signal path 4 will change substantially, while those of signal path 6 will vary only slightly. The amplitude determined by measuring circuit A will therefore fall to a minimum A0 at f0, as shown in Fig. 5. At the same time, phase shift phi crosses zero.

As can be shown, the dependence of A0 on the dielectric constant $\varepsilon(f)$ and, in particular, on the loss or conductance $\rho(f)$ of the fluid in the specimen is stronger than at off-resonance frequencies, which allows a sensitive measurement of the liquid's response to the electric field.

This is shown in Fig. 8, which represents measurements of the type shown in Fig. 5 at glucose concentrations between 0 and 17.5 mmol/l. The vertical axis represents the ratio in dB of the signals from first signal path 4 and second signal path 6. The resonance frequency is around 35.5 MHz.

It is presently believed that the specific impedance of the body fluid, i.e. the specific conductivity $\rho(f)$ and the dielectric constant $\varepsilon(f)$ in a frequency range between 10 MHz and 2000 MHz, and in particular between 20 MHz and 70 MHz, are a function of the properties and concentration of the salty (ionic) components of the human body. These salty components primarily include solvated sodium, potassium, calcium and other minor ions and their counter ions, the primary counter ion being chloride. Other non-ionic solvated substances, in particular substances having a similar range of size as the ion com-

25 arranged in an opening 26 of bottom electrode 22 on inner side 21.

Temperature sensor 10 is mounted to bottom electrode 22. The large number of through-contacts 23 ensure that bottom electrode 22 follows the temperature of ring electrode 18 and therefore the temperature of the specimen closely.

A typical size of electrode plate 14 is 32 mm x 21 mm. Bottom electrode 22 covers all of inner side 21 except for the small opening 26 and is therefore much larger than strip electrode 18.

Leads 28 are provided to connect bottom electrode 22, contact pad 26 and temperature sensor 10 to the electronic circuits 16.

While bottom electrode 22 and ring electrode 19 are connected to ground, strip electrode 18 is connected to inductance L of resonant circuit 5. Therefore, the capacitor C is formed between strip electrode 18 as a first electrode and ring electrode 19 and bottom electrode 22 as a second electrode. In other words, the second electrode consists of two electrode layers: a top electrode layer formed by ring electrode 19 and a bottom electrode layer formed by bottom electrode 22.

An electrically insulating cover layer 29 covers all of strip electrode 18 but not ring electrode 19. In other words, strip electrode 18 is arranged between substrate 17 and cover layer 29. Cover layer 29 is preferably of a hard, moisture- and salt-impervious material such as glass, ceramics, a polycarbonate or diamond-like carbon (DLC) of a thickness preferably between 50 and 100 µm.

As can be seen in Fig. 4, a holder or wristband 31 is attached to housing 13 for fixing the device to an arm or a leg of a human body with cover layer 29 facing the body and a longitudinal axis of strip electrode 18 parallel to the arm or leg. In this way, ring electrode 19 comes into contact with the user's skin and

A possible arrangement of the electrodes is shown in Fig. 7. As can be seen, antenna electrode 33 is strip shaped and arranged in parallel to strip electrode 18. Both, antenna electrode 33 and strip electrode 18 are covered by cover layer 29 and therefore electrically insulated from the specimen.

The device of Figs. 6 and 7 is again sweeping VCO 1 between a frequency fmin below the resonance frequency f0 of resonant circuit 5 and a frequency fmax above it. In contrast to Fig. 5, measuring circuit 7 now detects a maximum amplitude A0 at f0, wherein the value of A0 depends on the response, i.e. the electrical properties of the specimen at the resonance frequency f0. The parameter A0 can now again be processed using calibration data as described above.

A comparison of the device of Figs. 1 and 2 with the device of Figs. 6 and 7 shows that the first embodiment measures the response of the specimen from the signal reflected to strip electrode 18. The second embodiment measures the response of the specimen from the signal transmitted from strip electrode 18 to antenna electrode 33.

It is found that the transmission and reflection show different dependencies on the concentrations of various compounds of the body fluid. Hence, a combined measurement of reflection and transmission allows a further refinement of the measurement by elimination of the influence of compounds not of interest for the quantity to be measured.

A third embodiment of a circuit is shown in Fig. 9. Here, the capacitor C formed by the electrodes is part of the resonant tank circuit of an active, self-oscillating oscillator 40. The amplitude A and frequency f0 of the output signal of oscillator 40 depend on the capacitance and losses in capacitor C. The corresponding signal is fed to measuring circuit 7, which evaluates the parameters A and f0. Measuring the corresponding parame-

Claims

1. A method for determining the concentration of a substance in a in-vitro or in-vivo specimen containing body liquid comprising the steps of

arranging a first electrode (18) at said specimen, wherein said first electrode is electrically insulated from the specimen,

applying a modulated electrical voltage to the first electrode for generating a modulated field in the specimen and

measuring at least one parameter (A, phi) depending on a response of the specimen to the field and determining the concentration therefrom.

2. The method of claim 1 comprising the step of arranging a second electrode (19, 22) at said specimen, wherein the modulated electrical voltage is applied between the first and the second electrode (19, 22).

3. The method of claim 2 wherein the second electrode (19, 22) is in electric contact with the body liquid in the specimen.

4. The method of one of the preceding claims further comprising the step of measuring a temperature (T) of the specimen and using the temperature in the determination of the concentration.

5. The method of one of the preceding claims wherein the modulated electrical voltage is a sine voltage.

6. The method of one of the preceding claims wherein the modulated electrical voltage has a frequency between 10 MHz and 2 GHz, in particular between 20 MHz and 70 MHz.

7. The method of one of the preceding claims wherein the parameter (A, phi, f0) depends on the electrical impedance at the first electrode.

a first electrode (18) covered by a cover layer (29) of insulating material,

a signal source (1) connected to the first electrode (18) applying a modulated electrical voltage to the first electrode (18) for generating an electric field in the specimen,

a measuring circuit (7) for measuring at least one parameter depending on a response of the specimen to the field, and

a data processor (8) determining the concentration from the parameter.

17. The device of claim 16 comprising a holder (31) for fixing the first electrode (18) to a part of a body with the cover layer (29) facing the body.

18. The device of one of the claims 16 or 17 further comprising an electrically insulating substrate (17), wherein the first electrode (18) is arranged on a first side (20) of the substrate (17) between the substrate (17) and the cover layer (29).

19. The device of claim 18 further comprising a second electrode (19, 22) arranged on the substrate, wherein the signal source (2) is connected to apply the modulated electrical voltage between the first (18) and the second (19, 22) electrode.

20. The device of claim 19, wherein the second electrode (19, 22) comprises a bottom electrode layer (22) arranged on a second side (21) of the substrate (17), said bottom electrode layer (22) having a larger extension than said top electrode layer (18).

21. The device of one of the claims 19 or 20, wherein the second electrode (19, 22) comprises a top electrode layer (19) arranged on the first side (20) of the substrate (17), said top electrode layer (19) being arranged around at least part, in particular substantially all, of the first electrode (18).

of the first electrode being substantially parallel to the arm or leg

a signal source connected to the first electrode applying a modulated electrical voltage to the first electrode (18) for generating a modulated field in the specimen,

a measuring circuit (7) for measuring at least one parameter (A, phi, f0) depending on a response of the specimen to the field, and

a data processor determining the concentration from the parameter.

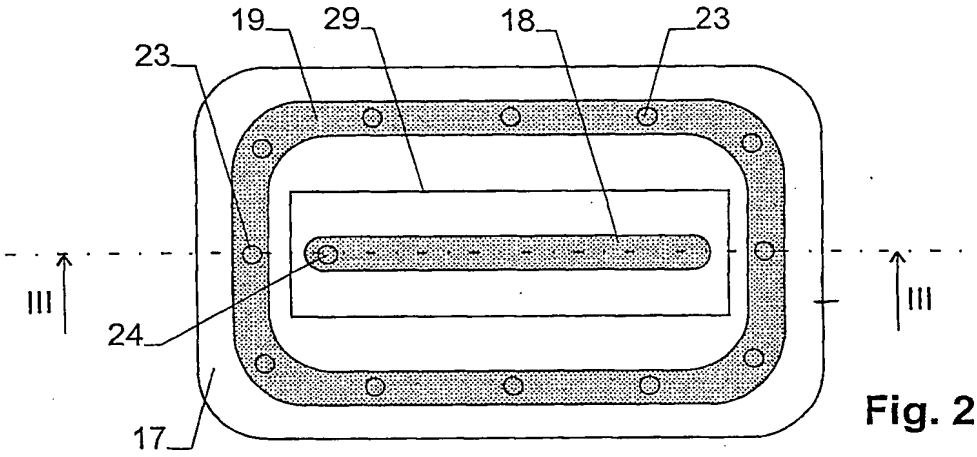


Fig. 2

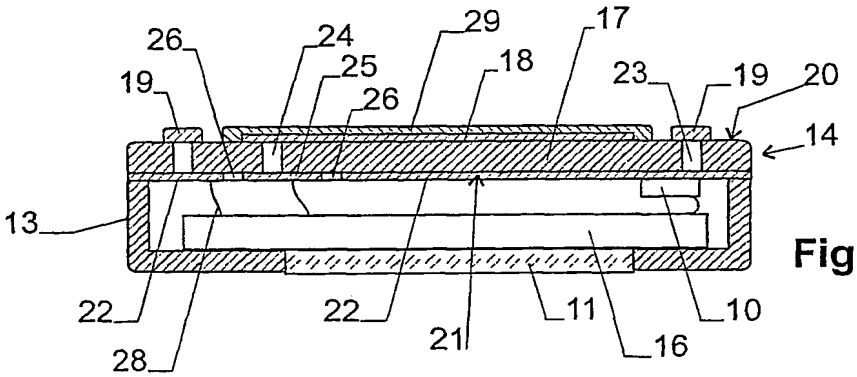


Fig. 3

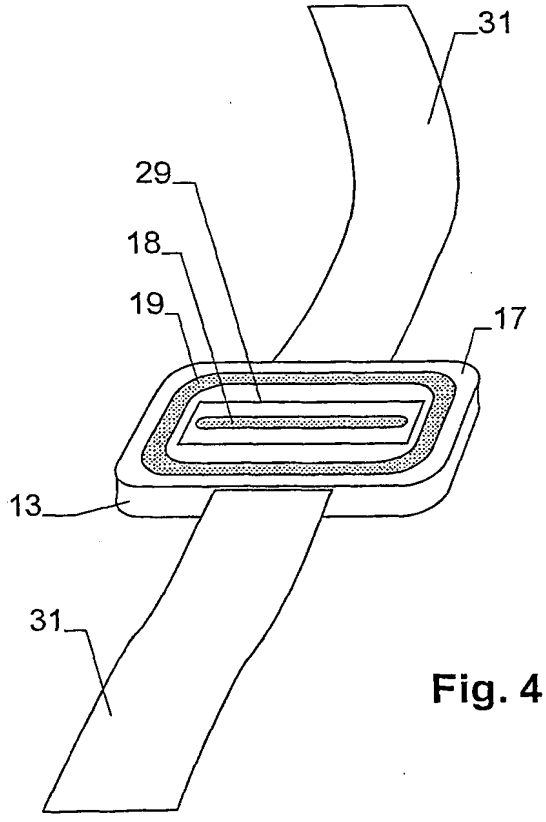
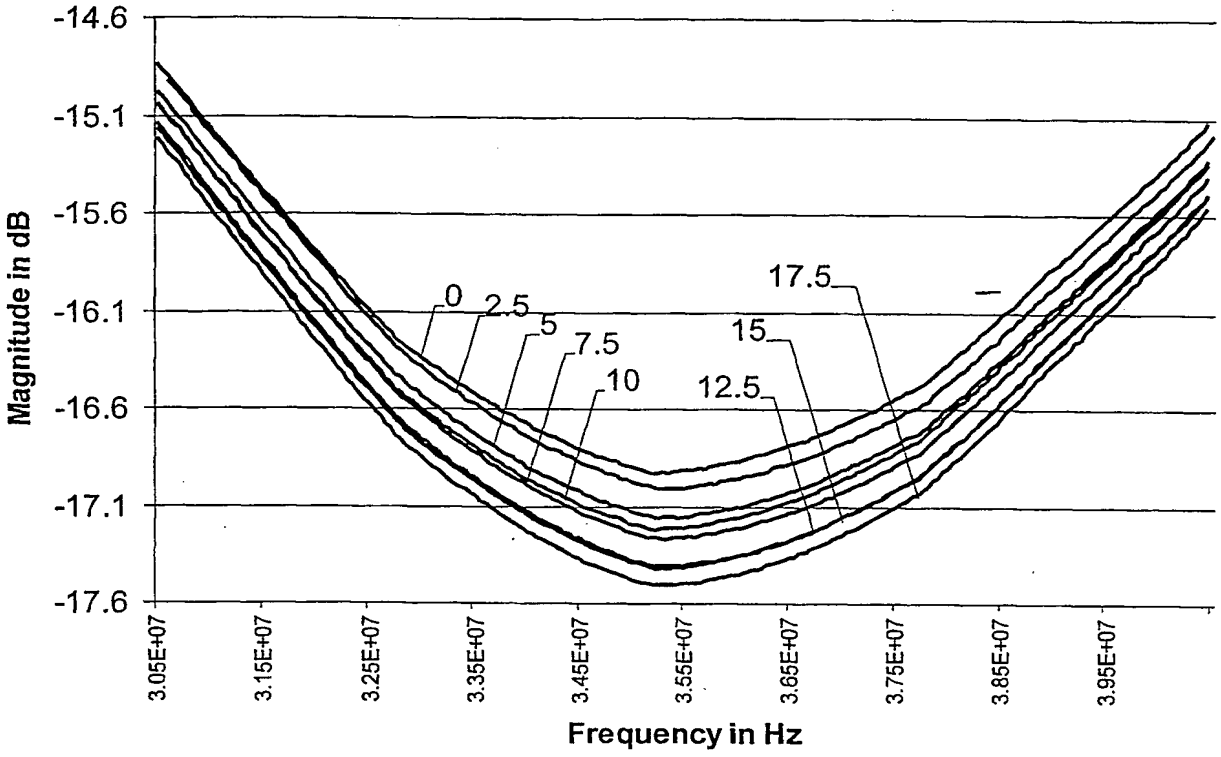


Fig. 4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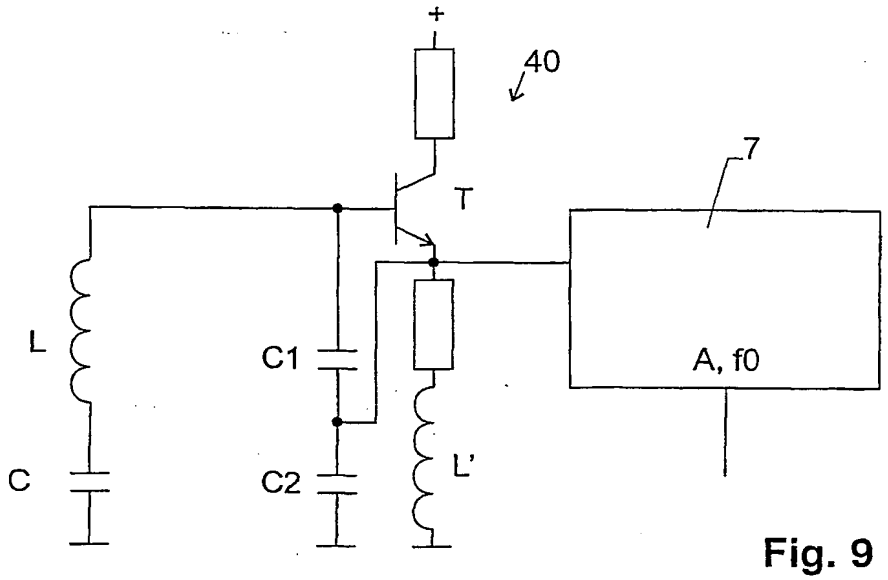
3.65E+07
3.75E+07
3.85E+07
3.95E+07
Frequency in Hz

Fig. 8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A, f0
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Fig. 9

INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 509 531 A (WARD JOHN W) 9 April 1985 (1985-04-09) abstract; figures 1-3	
A	WO 85 04481 A (HEALTH LAB SERVICE BOARD) 10 October 1985 (1985-10-10) abstract	